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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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[REDACTED] EXAMINER

AFREMOVA, VERA

[REDACTED] ART UNIT      [REDACTED] PAPER NUMBER

1651

DATE MAILED: 12/27/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/755,205</b>	Applicant(s) <b>Yang et al</b>
	Examiner <b>Vera Afremova</b>	Art Unit <b>1651</b>



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1)  Responsive to communication(s) filed on Oct 7, 2002

2a)  This action is FINAL.      2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

#### Disposition of Claims

4)  Claim(s) 10-43 is/are pending in the application.

4a) Of the above, claim(s) 10-35 is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 36-43 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.

2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1)  Notice of References Cited (PTO-892)

4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)

5)  Notice of Informal Patent Application (PTO-152)

3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_

6)  Other: \_\_\_\_\_

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## **DETAILED ACTION**

New claims 36-43 are under examination in the instant office action [Paper No. 11 filed 10/07/2002].

Claims 1-4 and 9 are canceled by applicants [Paper No. 11 filed 10/07/2002]. Claims 5-8 are canceled by applicants in the Paper No. 9 filed 3/25/2002. Claims 10-35 are withdrawn from consideration as being directed to non-elected invention [Paper No. 8 filed 3/20 2002 and Paper No. 10 mailed 7/02/2002].

### ***Response to Arguments***

Applicants' arguments filed 10/07/2002 have been fully considered but they are not persuasive for the reasons below.

### ***Claim Rejections - 35 USC § 112***

#### ***Indefinite***

New claims 336-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 43 are rendered indefinite by the phrase "substantially" in the lack of particular definitions related to a "substantially" stationary solid surface, even when reading the claims in the light of the specification. See also new matter rejection.

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*New matter*

New claims 36-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation directed to the use of “substantially stationary” solid surface has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept of the use of “substantially stationary” solid surface in the method for cryopreservation of biological material. There is a description of a Figure 1 (specification page 13, par. 2 ). But it does not provide disclosure about how or whether the metal cube or the aluminum foil is “substantially stationary” as required by the presently claimed invention. This is not sufficient support for the new genus as claimed. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of the limitation directed to the use of “substantially stationary” solid surface is considered to be the insertion of new matter for the above reasons.

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***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New claims 36-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,780,295 [IDS-4-2] taken with Steponkus et al. [IDS-4-6], Martino et al. [IDS-5-11], Yang et al. [IDS-5-21] and Papis et al. [IDS-5-22] as explained in the prior office action and for the reasons below.

Claims are directed to a method for vitrification and cryopreservation of biological material wherein the method comprises step of suspending the biological material in a cryopreservation and/or vitrification solution and step of directly contacting the droplets of the suspended biological material with a cold solid surface which has thermal conductivity and which has temperature of about - 150°C to about - 180°C. The droplets have size of about 10 µL and less. The conductivity of the solid surface has a particular value. Some claims are further drawn to the use of biological material such as cells, oocytes or embryos.

The cited references are relied as explained in the prior office action and repeated herein. US 5,780,295 [IDS-4-2] teaches a method for vitrification and cryopreservation of biological material wherein the method comprises step of suspending and rinsing the biological material in solutions containing cryoprotectants, step of dropping the solutions with the biological material in a form of micro droplets onto a solid cryogenic surface which is cooled to about - 160°C (col. 4, lines 17-24). The cited patent teaches the use of a cryogenic surface which

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has high thermal conductivity as metal and which allows to achieve high cooling rate and to avoid thermal shock of biological material (col. 7, lines 7-12). The cited patent teaches the use of micro droplets which have size of about 25  $\mu\text{L}$  to about 250  $\mu\text{L}$  and it teaches that the smaller size is preferential in order to achieve maximum cooling rate and short drying time (col.6, lines 32-37). The patent discloses the use of various biological materials including cells, sperm and isles (col. 4, lines 55-60) and the use of various solutions with cryoprotectant at various concentration suitable in the method for vitrification and cryopreservation of biological material (col. 8).

The cited patent US 5,780,295 [IDS-4-2] discloses the use of various biological materials including cells, sperm and isles (col. 4, lines 55-60) but it lacks particular disclosure related to the oocytes and embryos.

The cited patent US 5,780,295 [IDS-4-2] teaches the use of rotating cold surface but not a stationary surface and is lacking the disclosure about the use of droplets with size of 10  $\mu\text{L}$  or less.

However, the references by Steponkus et al. [IDS-4-6] (see description under fig. 1) and Martino et al. [IDS-5-11] (see abstract and page 1061, col. 1, last paragraph) disclose methods for vitrification and cryopreservation of embryos and oocytes wherein the method comprises steps pretreatment of biological materials with cryopreservation and vitrification solutions at particular concentrations suitable for vitrification and cryopreservation of embryos or oocytes and step of dropping the suspended biological material including embryo or oocytes in a form of

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micro droplets onto a stationary solid copper surface which is plunged into liquid nitrogen. The reference by Steponkus et al. teach the use of micro droplets having size of about 20 µL for biological material comprising eggs or embryos. The reference by Martino et al. teach the use of micro droplets having size of less than 1 µL for biological material comprising oocytes

The other cited references by Yang et al. [IDS-5-21] and Papis et al. [IDS-5-22] are relied upon for the disclosure of methods for vitrification and cryopreservation of biological material including mammalian oocytes and zygotes by ultra-rapid cooling intended to avoid chilling injury of the biological material wherein the methods encompasses the use of cryoprotective equilibration solution and vitrification solution for suspending of the biological material prior cooling/cryopreservation and the use of the suspended micro droplets having various sizes depending on type of biological material such as about 10 µL for bovine zygotes and about 6 µL for bovine oocytes (see abstracts).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to substitute oocytes or embryos of the secondary references [Steponkus et al., Martino et al., Yang et al., Papis et al.] for a generic biological material in the method for vitrification and cryopreservation of US '295 which encompass the ultra-rapid cooling on a solid cryogenic surface with a reasonable expectation of success in vitrification and cryopreservation of oocytes and/or embryos because it is known to freeze oocytes and embryos on solid copper grids designed for ultra-rapid cooling [Steponkus et al., Martino et al.] which allows to avoid chilling injury and obtained satisfactory results for future oocyte fertilization and

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embryo development as taught by the secondary references [Steponkus et al., Martino et al., Yang et al., Papis et al.]. One of skill in the art would have been motivated to decrease sizes of micro droplets because the prior art teaches that the smaller size is preferential in order to achieve maximum cooling rate and short drying time [US'295] and the use of micro droplets of sizes such as about 10  $\mu\text{L}$  and less have been demonstrated in the prior art [Martino et al., Yang et al., Papis et al.]. Although the cited references are silent with regard to a particular value of the thermal conductivity of solid surfaces used in the method for cryopreservation, the materials which are used are metals and they are characterized by high thermal conductive properties sufficient to achieve rapid cooling and to avoid chilling injury of biological materials as taught by the references. The particular heat conductivity which is claimed is the same as that of a metal (specification page 7, line 7). Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

With regard to the cited patent US 5,780,295 [IDS-4-2] applicants appear to argue that it distinguishes over the claimed invention because it teaches step of nebulizing the solution with the biological material and/or the use of a nebulizer to deliver the biological material to the cold surface (response page 4, par. 1). Yet, the claimed method does not exclude the use of a nebulizer

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or a nebulizing step by the virtue of the open language “comprising”. Moreover, the claimed method requires the use or formation of micro droplets as clearly taught by the cited reference.

With regard to the cited patent US 5,780,295 applicants also argue that the cold solid surface in the cited method is rotating rather than “substantially stationary” (response page 4, par. 1-2). Yet, it is uncertain what is encompassed by “substantially stationary” in the presently claimed invention as discussed above. Further, this argument appears to be drawn to a particular design of an apparatus rather than to a method of cryopreservation of biological material. It can not be ascertained from the record whether the movement of apparatus/surface materially affects the viability of the cryopreserved biological material. Therefore, whatever differences might exist between “rotating” and “substantially stationary” solid surfaces used for cooling and cryopreserving, are not considered to clearly patentably distinguish between the presently claimed method and the cited method of US'295 for cryopreservation of biological material. Moreover, the other prior art references teach the use of stationary solid surfaces or copper grids which are plunged into liquid nitrogen for cryopreserving biological material. For example: see the reference by Steponkus et al. [IDS-4-6] at Fig. 1, line 24-26, technique #5. See abstract of the reference by Martino et al. [IDS-5-11].

Applicants also appear to argue the criticality of size of droplets with biological materials (response page 5). However, this concept is taught and suggested by the prior art of record as demonstrated by the cited references combined. For example: the cited US'295 teaches that the use of a smaller size is preferential in order to achieve maximum cooling rate and short drying

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time and the use of micro droplets of sizes such as about 10 µL and less have been demonstrated by the references by Martino et al., Yang et al., and Papis et al. In the method for cryopreservation of biological material.

The references by Yang et al. [IDS-5-21] and Papis et al. [IDS-5-22] are the prior art references in the claim rejection under 35 U.S.C. 103(a) as set forth in section 102 (a) because they are references published by others before the invention thereof by applicants for a patent.

No claims are allowed.

*Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

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December 20, 2002.

PRIM EXAMINER  
Irene Marx  
IRENE MARX  
PRIMARY EXAMINER